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EXAMINER	
CHEU, CHANGHWA J	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,104	GOLZ ET AL	
	Examiner	Art Unit	
	JACOB CHEU	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Applicant's amendment filed on 2/13/2008 has been received and entered into record and considered.

The following information provided in the amendment affects the instant application:

1. Claims 1, 3-23 have been cancelled.
2. Claim 24 has been added.
3. Currently, claim 2 and 24 are under examination.

Claim Rejections - 35 USC § 112

Enablement

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 2 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in *In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)*, enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art,

3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The instant invention provides a human NPEPPS which is associated with the cardiovascular diseases, dermatological diseases, endocrinological diseases, metabolic diseases, cancer, gastroenterological diseases, muscle-skeleton diseases, neurological diseases, respiratory diseases, inflammation and urological diseases. The instant invention directs to a screening assay for the identification of compounds useful in the treatment or prevention of cardiovascular diseases, dermatological diseases, endocrinological diseases, metabolic diseases, cancer, gastroenterological diseases, muscle-skeleton diseases, neurological diseases, respiratory diseases, inflammation and urological diseases.

However, in view of the data provided by applicants, one ordinary skill in the art would not conclude that merely identifying compounds capable of modulating NPEPPS polypeptide activity would be sufficient as a "useful" treatment to the above mentioned disease. It is noted that applicant conducted analysis of tissues obtained from various patients suffered from different diseases and compared to normal/or symptom-free control (See Table 1; See Section 0042-0045). The results indicate some difference, either higher or lower of the expression of the NPEPPS *mRNA* in the patients' tissue compared with the normal samples from the symptom free people (emphasis added). Supra. Examiner acknowledges that NPEPPS would be considered a biomarker for disease *diagnosis* based on data of Table 1 because the different profile of expression in various condition, including normal and pathological state tissues (emphasis added). Nevertheless, without further research or confirmation, it would be a far-fetch to conclude that NPEPPS is a target molecule for "useful treatment" for the above mentioned diseases by merely identifying agents or compounds "regulating", i.e. up-regulation or down-regulation, the NPEPPS protein in the specific tissues.

The up-regulation (e.g. higher level) or down-regulation (e.g. lower level) of a particular protein for a particular disease does not warrant a causal-link that modulation of said particular protein is

the key for successful treatment. Applicant also does not provide ANY treatment data with respect to ANY recited disease. Furthermore, no example and no guidance is provided as to the evaluation of the success of the treatment. For example, no particular markers or functionality test of a particular disease have been mentioned as to the evaluation criteria. In another word, no disclosure of how one ordinary skill in the art in view of the data would extrapolate to a successful treatment to the instant recited disease. Moreover, it is known that not every overexpressed protein is the cause of the disease. For instance, Sakoda et al. found out that PC-1 protein is overly expressed in the insulin resistance patients. However, SaKoda et al. disclose that the increased PC-1 expression is not casually related to insulin resistance (See Sakoda et al. Diabetes 1999 Vol. 48, page 1365-1371; whole document, particularly Abstract). Similarly, Laurentiis et al. also observe that overly expressed HER-2 metastatic breast cancer would not respond to endocrine treatment, albeit with positive endocrine estrogen receptor expression (See Laurentiis et al. Clin Cancer Res 2005 Vol. 11, page 4741-4748; See Abstract). In addition, applicant had not disclosed the nexus between the NPEPPS and the cause of the disease. It is not known what is the relationship between the activity of the NPEPPS and the occurrence or development of the recited disease. Applicant had not disclosed any particular portion(s) of the NPEPPS responsible with its activity and related to any recited disease. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) , the court indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. As discussed earlier, thus far, applicant merely provides data with respect to difference of the NPEPPS expression in various tissues from the recited patients. At most, it is a diagnosis method for identifying the recited diseases. Nevertheless, there exists a unpredictable gap between extrapolation from diagnosis to treatment, and applicant's data are not sufficient to bridge such gap.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 2 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Yang et al. (WO 01/46443; applicant's IDS reference).

> Yang et al. disclose a method of screening for therapeutic agents for treatment of disease. Yang et al. teach determining the activity of a NPEPPS polypeptide, i.e. SEQ 9 (which is identical to the recited *SEQ ID No. 2*), in the absence or presence of the test compound at different concentrations (See page 82, Section XIX; claims 1, 16, 19 and 22). The compounds tested can be used for treatment of inflammation, cancer, infection, cardiovascular, neurological, endocrinological or metabolic diseases (See page 41-44).

8. Claims 2 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Fontana et al. (WO 97/38114; applicant's IDS reference).

> Fontana et al. disclose a method of screening for therapeutic agents for treatment of disease. Yang et al. teach determining the activity of a NPEPPS polypeptide, i.e. SEQ 6 (which is identical to the recited *SEQ ID No. 2*), in the absence or presence of the test compound at different concentration (See page 51, second paragraph, page 72, third paragraph; claims 1, 23-24). The compounds tested can be used for treatment of inflammation and cancer, (See page 51-52).

Response to Applicant's Arguments

9. The rejection of claim 2 under 35 USC 112, first paragraph written description is withdrawn because specification provides support for the recited invention.

10. The enablement rejection of claim 2 under 35 USC 112, first paragraph is maintained.

Applicant argues that the Office faults with such rejection because specification do not need to provide information with respect to the treatment data. Applicant also argues that the claim does not require that identified compound be useful to treatment, rather the claim is directed to a method of screening for therapeutic agents useful in treatment. Such method only needs to identify the compounds of potential use in the treatment (See Remarks, page 5).

Applicant's arguments have been considered, but are not persuasive.

As indicated in the Office Action, the disclosure of the current specification merely shows the different mRNA expression of the NPEPPS, in various normal and pathological tissues. Applicant has not provided sufficient information with respect to the nexus between the mRNA of NPEPPS and the pathological state of the various diseases. Examiner acknowledges that the distinct appearance of NPEPPS, e.g. downregulated or upregulated, in the pathological tissues, may potentially serve as a biomarker of diagnosis. However, researchers in the field have established the gap or lack of causal-link, between the diagnosis to useful treatment (See above). Reaching to the useful treatment with specified compound(s) in relation to a particular disease, is not a simple task merely by identifying modulating compound to certain upregulated or downregulated tissue protein. Accordingly, the claim does not satisfy the enablement criteria set forth in the 35 USC, 112, first paragraph.

11. The rejection of claim 2 as anticipated by Yang et al. under 35 USC 102 (b) is maintained.

Applicant argues that Yang et al. teaches 28 proteins and do not explicitly teach screening for therapeutic agents useful in the treatments of the diseases.

Applicant's arguments have been considered, but are not persuasive.

Contrary to what asserted by Applicant, Examiner would like to draw Applicant's attention to claims 1, 19 and 22 of Yang et al. reference. Yang et al. teach in claim 1, a polypeptide comprising SEQ ID Nos. 1-14 where the SEQ ID No. 9 is the same as the recited SEQ ID NO. 2. In claim 19, Yang et al. teach a method of screening a compound as agonist of the polypeptide of claim 1, and claim 22 directs to a screening method identifying an antagonist of the polypeptide of claim 1. Both agonist and antagonist are modulating agents of the polypeptides of claim 1. The compounds tested can be used for treatment of inflammation, cancer, infection, cardio-vascular, neurological, endocrinological or metabolic diseases (See page 28, line 25-33; page 41-44). Particularly, page 28, Yang et al. states *"[t]he invention is based on the discovery of new human proteases (PRTS), the polynucleotides encoding PRTS, and the use of these compositions for the diagnosis, treatment, or prevention of gastrointestinal, cardiovascular, autoimmune/inflammatory, cell proliferative, developmental, epithelial; neurological, and reproductive disorders."* Thus, the teachings of Yang et al. anticipate the instant invention.

12. The rejection of claim 2 under 35 U.S.C. 102(b) as being anticipated by Fontana et al. is maintained.

Similarly, Applicant argues that Fontana et al. do not explicitly teach the treatment of the disease, and no data correlating expression of the protein with tissues relevant to these diseases. Applicant also indicates that no experiments were actually carried out. Thus

one ordinary skill in the art would not use the proteins taught by Fontana et al. to screen potential compounds in treating with the diseases.

Applicant's arguments have been considered, but are not persuasive.

As pointed out by the Examiner, Fontana et al. in fact disclose the recited method of screening potential compounds for the treatment of various diseases. In page 39, first paragraph, Fontana et al. states *"[T]he compounds of the present invention, due to their ability to diminish the PSA activity in cells by modulation of the amount of PSA being present in the cells due to modulation of its synthesis, especially inhibition thereof, are effective in the treatment of proliferative and especially hyperproliferative diseases, preferably tumor diseases, especially leukemias; tumors of the prostate, such as prostatic carcinoma; tumors of the colon; brain tumors; hyperproliferative skin and epithelial diseases, for example psoriasis."*(emphasis added) It is clearly in Fontana's contemplation to apply the SEQ ID No. 6 (which is the current recited SEQ ID No. 2) for screening of therapeutic to identify treatment, such as dermatological diseases (Applicant's recited disease). Thus, the reference taught by Fontana et al. anticipates the instant invention.

Conclusion

13. No claim is allowed.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jacob Cheu/
Examiner, Art Unit 1641

/Long V Le/
Supervisory Patent Examiner, Art Unit 1641